Integrative Multi-omics Analysis Identifies Histone Methyltransferase SUV420H2 as a Prognostic Biomarker in Clear Cell Renal Cell Carcinoma

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DEGs in selected cancer types

PRDM12
EZH2
SMYD2
PRDM1
SMYD4
KMT5C
SETD7
SETD1A
PRMT3
PRDM4
SETD1B
KMT2D
KMT2C
SMYD5
SUV39H1
SETDB1
PRMT1
DOT1L
KMT2E
PRMT7
CARM1
PRDM15
EHMT2
PRMT2
SUV39H2
SMYD1
SETD5
PRDM9
PRDM13
KMT2A
EHMT1
PRDM10
NSD1
SETDB2
SETD3
SETMAR
KMT5B
PRMT5
SETD2
PRDM5
EZH1
PRDM11
ASH1L
SMYD3
PRDM2
PRMT8
PRDM14
PRMT6
PRDM7
PRDM16

Gene symbol

KIRC
KIRP
KICH

Cancer

log2(FC)
6
0
−6

−Log10(FDR)
10
20
30

FDR
<=0.05
>0.05

Figure S1. Differential expression landscape of selected histone methyltransferases across RCC subtypes. Differential expression analysis of histone methyltransferases (HMTs) in clear-cell renal cell carcinoma (KIRC), papillary renal cell carcinoma (KIRP), and chromophobe renal cell carcinoma (KICH) compared with corresponding normal tissues. Log2 fold-change values are represented along the x-axis, while statistical significance is shown as –log10(FDR). Red colour indicates significantly upregulated genes (FDR ≤ 0.05), whereas purple represents downregulated (FDR ≤ 0.05) genes; grey dots represent non-significant genes.

ENSG00000005483.19 (KMT2E)
ENSG00000055609.17 (KMT2C)
ENSG00000167548.14 (KMT2D)
ENSG00000118058.20 (KMT2A)
ENSG00000142611.16 (PRDM16)
ENSG00000141956.13 (PRDM15)
ENSG00000147596.3 (PRDM14)
ENSG00000112238.11 (PRDM13)
ENSG00000130711.3 (PRDM12)
ENSG00000019485.12 (PRDM11)
ENSG00000170325.14 (PRDM10)
ENSG00000164256.9 (PRDM9)
ENSG00000126856.13 (PRDM7)
ENSG00000138738.10 (PRDM5)
ENSG00000110851.11 (PRDM4)
ENSG00000116731.22 (PRDM2)
ENSG00000057657.14 (PRDM1)
ENSG00000133247.13 (SUV420H2)
ENSG00000110066.14 (SUV420H1)
ENSG00000109685.17 (WHSC1)
ENSG00000147548.16 (WHSC1L1)
ENSG00000136169.16 (SETDB2)
ENSG00000143379.12 (SETDB1)
ENSG00000170364.12 (SETMAR)
ENSG00000183955.12 (SETD8)
ENSG00000145391.13 (SETD7)
ENSG00000168137.15 (SETD5)
ENSG00000139718.10 (SETD1B)
ENSG00000099381.16 (SETD1A)
ENSG00000101945.16 (SUV39H1)
ENSG00000152455.15 (SUV39H2)
ENSG00000116539.10 (ASH1L)
ENSG00000204371.11 (EHMT2)
ENSG00000181090.17 (EHMT1)
ENSG00000108799.12 (EZH1)
ENSG00000106462.10 (EZH2)
ENSG00000104885.17 (DOT1L)
ENSG00000183576.12 (SETD3)
ENSG00000181555.19 (SETD2)
ENSG00000165671.18 (NSD1)
ENSG00000111218.11 (PRMT8)
ENSG00000132600.16 (PRMT7)
ENSG00000198890.7 (PRMT6)
ENSG00000100462.15 (PRMT5)
ENSG00000142453.11 (CARM1)
ENSG00000185238.12 (PRMT3)
ENSG00000160310.16 (PRMT2)
ENSG00000126457.20 (PRMT1)
ENSG00000135632.11 (SMYD5)
ENSG00000186532.11 (SMYD4)
ENSG00000185420.18 (SMYD3)
ENSG00000143499.13 (SMYD2)
ENSG00000115593.14 (SMYD1)

log10(HR)
1.0
0.5
0.0
−0.5
−1.0

KICH
KIRC
KIRP

Figure S2: Screening of histone methyltransferases (HMTs) based on prognostic significance across RCC subtypes. Heatmap showing overall survival associations for HMTs using TCGA KIRC, KIRP and KICH datasets. Hazard ratios, log-rank p-values, and significance levels are displayed. Genes marked with red boxes represent the statistically significant most clinically relevant HMTs associated with poor overall survival. These genes were shortlisted for downstream evaluation. Genes marked with blue boxes represent statistically significant HMTs associated with better overall survival.

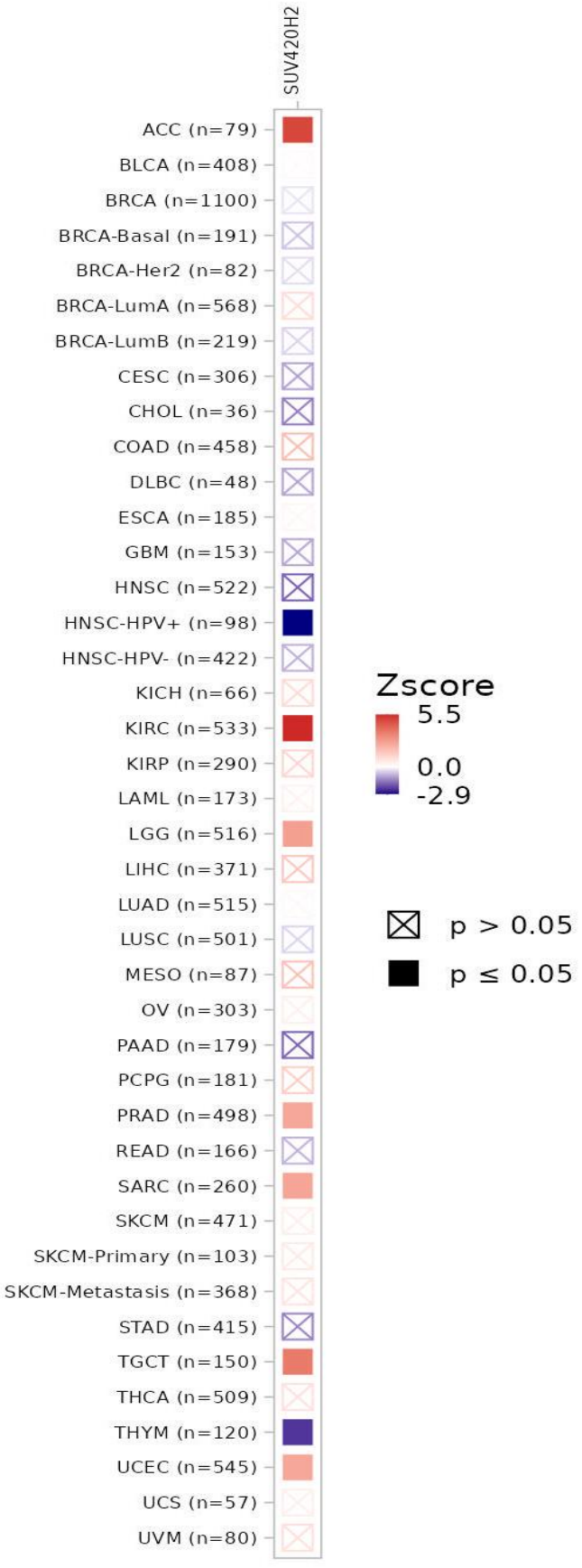
SUV420H2
ACC (n=79)
BLCA (n=408)
BRCA (n=1100)
BRCA-Basal (n=191)
BRCA-Her2 (n=82)
BRCA-LumA (n=568)
BRCA-LumB (n=219)
CESC (n=306)
CHOL (n=36)
COAD (n=458)
DLBC (n=48)
ESCA (n=185)
GBM (n=153)
HNSC (n=522)
HNSC-HPV+ (n=98)
HNSC-HPV- (n=422)
KICH (n=66)
KIRC (n=533)
KIRP (n=290)
LAML (n=173)
LGG (n=516)
LIHC (n=371)
LUAD (n=515)
LUSC (n=501)
MESO (n=87)
OV (n=303)
PAAD (n=179)
PCPG (n=181)
PRAD (n=498)
READ (n=166)
SARC (n=260)
SKCM (n=471)
SKCM-Primary (n=103)
SKCM-Metastasis (n=368)
STAD (n=415)
TGCT (n=150)
THCA (n=509)
THYM (n=120)
UCEC (n=545)
UCS (n=57)
UVM (n=80)
Zscore
5.5
0.0
-2.9
p > 0.05
p ≤ 0.05

Figure S3: Multivariate analysis of SUV420H2 overall survival in Pan-cancer. Multivariate Cox proportional hazards regression across TCGA cancer types showing Z-scores for the association between SUV420H2 expression and overall survival. Red indicates positive association (higher expression associated with poorer survival), while blue indicates negative association (higher expression associated with improved survival). Filled squares denote statistically significant associations ($p \leq 0.05$), whereas crossed squares indicate non-significant results ($p > 0.05$). Sample sizes for each cancer type are indicated in parentheses.

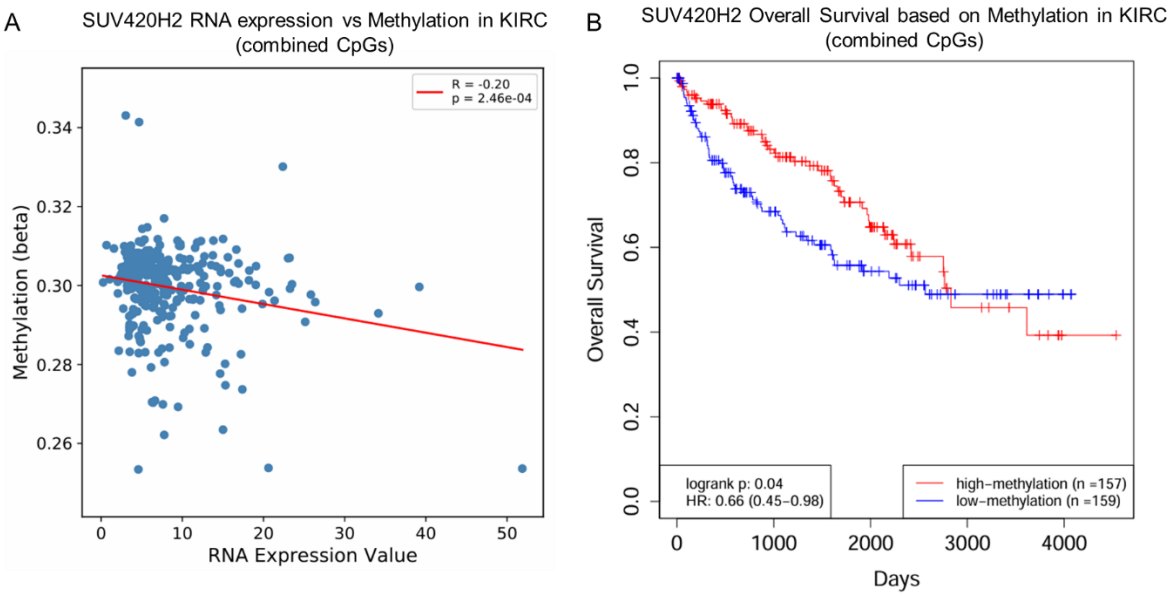

Figure S4: Association between SUV420H2 methylation and overall survival. [A] Spearman correlation between SUV420H2 methylation (combined CpGs) and mRNA expression; [B] Overall survival associated with SUV420H2 high and low methylation cohorts (combined methylation of all CpGs).

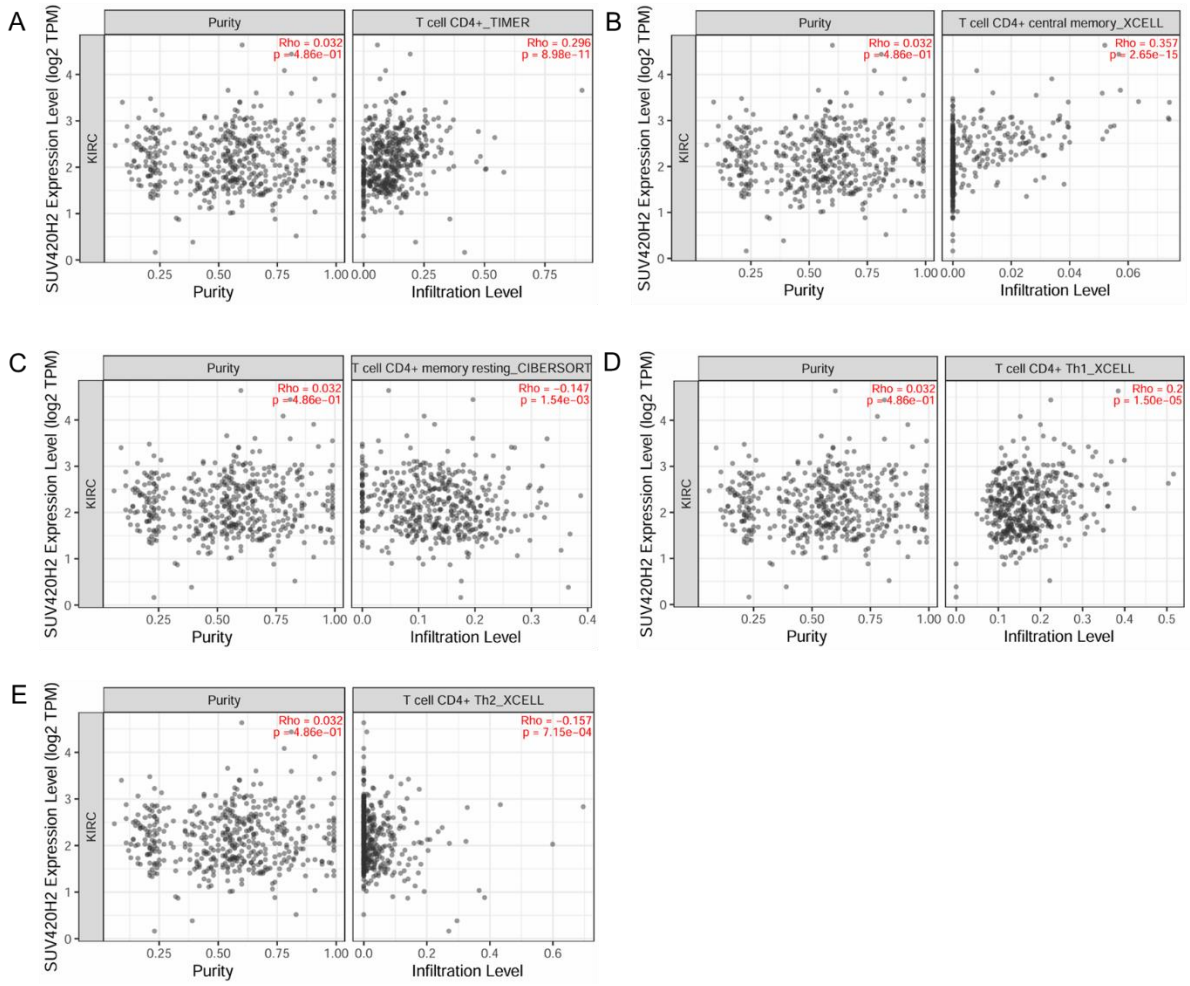

Figure S5: Association of SUV420H2 with CD4⁺ T-cell subsets across multiple immune deconvolution algorithms. [A] TIMER-based estimation showing correlation with total CD4⁺ T-cell infiltration and SUV420H2 expression; [B] xCell-based estimation showing correlation of central memory CD4⁺ T cells with SUV420H2 expression; [C] CIBERSORT-based estimation showing correlation between resting memory CD4⁺ T cells and SUV420H2 expression; [D] xCell-based estimation showing correlation between Th1 CD4⁺ T cells and SUV420H2 expression; [E] xCell-based estimation showing correlation between Th2 CD4⁺ T cells and SUV420H2 expression [Scatter plots show Spearman correlation coefficients (Rho) and corresponding p-values].

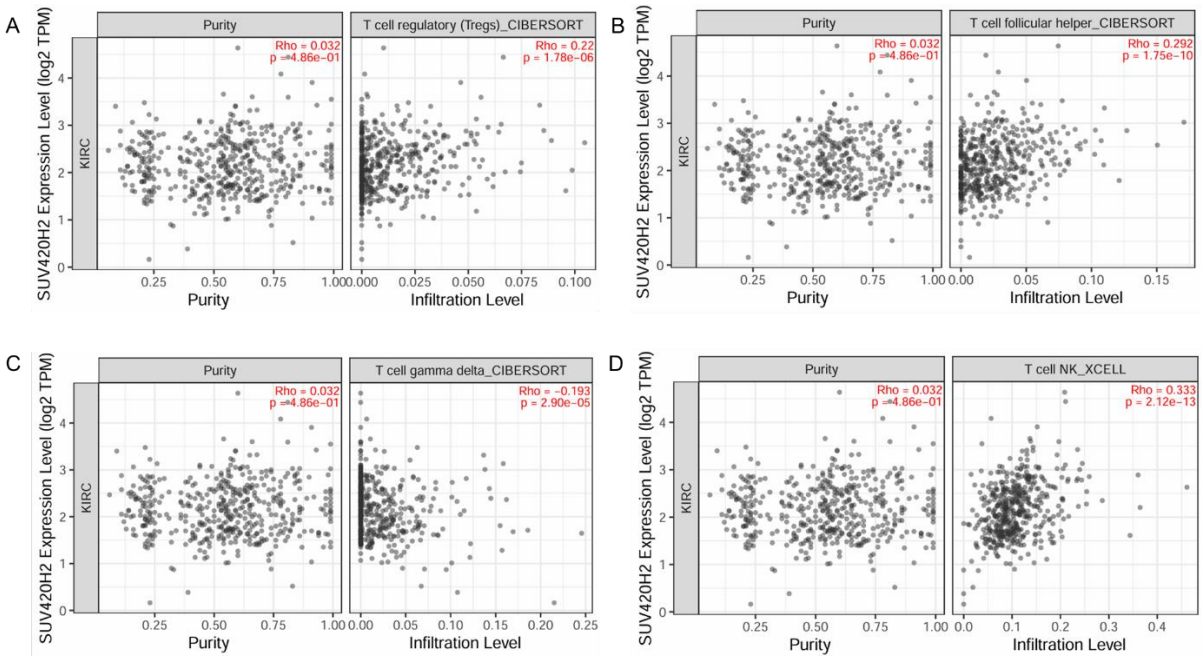

Figure S6: Association of SUV420H2 with regulatory and lymphoid immune cell populations. [A] CIBERSORT-based estimation showing correlation between regulatory T cells (Tregs) and SUV420H2 expression; [B] CIBERSORT-based estimation showing correlation between T follicular helper (Tfh) cells and SUV420H2 expression; [C] CIBERSORT-based estimation showing correlation between γδ T cells and SUV420H2 expression; [D] xCell-based estimation showing correlation between natural killer (NK) cells and SUV420H2 expression [Scatter plots display Spearman correlation coefficients (Rho) and p-values].

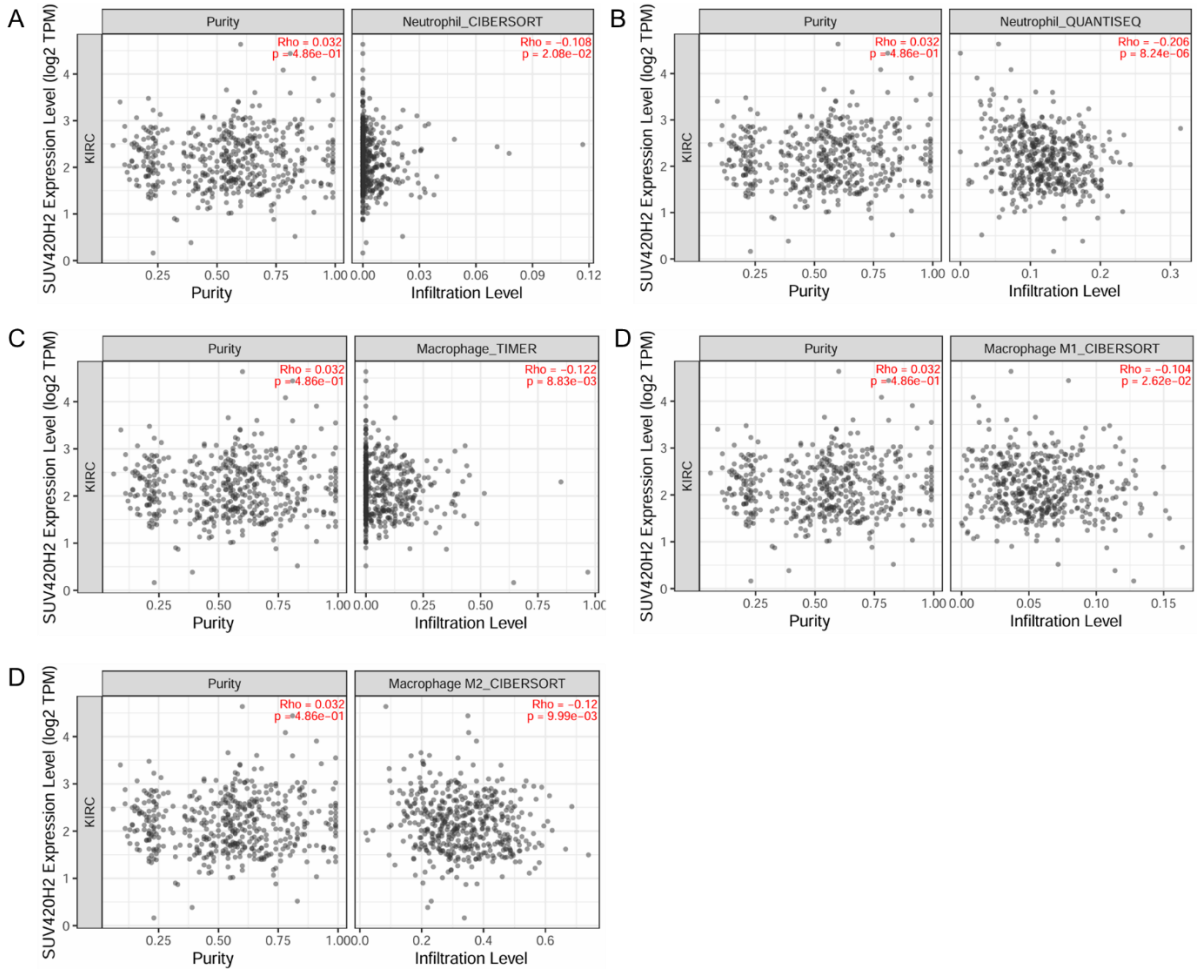

Figure S7: Association of SUV420H2 expression with myeloid immune cell infiltration across multiple algorithms. [A] CIBERSORT-based estimation showing correlation between neutrophil infiltration and SUV420H2 expression; [B] quanTIseq-based estimation showing correlation between neutrophil infiltration and SUV420H2 expression; [C] TIMER-based estimation showing correlation between macrophage infiltration and SUV420H2 expression; [D] CIBERSORT-based estimation showing correlation between M1 macrophages and SUV420H2 expression; [E] CIBERSORT-based estimation showing correlation between M2 macrophages and SUV420H2 expression [Scatter plots include Spearman correlation coefficients (Rho) and corresponding p-values].